(FILE 'HOME' ENTERED AT 21:52:44 ON 31 MAY 2003)

US 2002168736

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20021114

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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED
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             292 S TRANSGEN? (L) (SCURFY OR SF OR FKHSF)
             105 DUP REM L1 (187 DUPLICATES REMOVED)
L2
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L3
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L4
              43 FOCUS L4 1-
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L6
1.7
              17 S SCURFY (L) TRANSGENIC
1.8
                6 DUP REM L7 (11 DUPLICATES REMOVED)
                6 SORT L8 PY
1.9
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     ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AN
     2000:133832 CAPLUS
DN
     132:190512
ΤI
     Gene causing the mouse scurfy phenotype and its human ortholog
SO
     PCT Int. Appl., 59 pp.
     CODEN: PIXXD2
IN
     Brunkow, Mary E.; Jeffery, Eric W.; Hjerrild, Kathryn A.; Ramsdell, Fred
     The present invention relates generally to the discovery of novel genes
AB
     which, when mutated, results in a profound lymphoproliferative disorder.
     In particular, a mutant mouse designated Scurfy was used to identify the
     gene responsible for this disorder through backcross anal., phys. mapping,
     and large-scale sequencing. Isolated nucleic acid mols. are provided which encode Fkhsf, as well as mutant forms, which belongs to a family of
     related genes, all contg. a winged-helix DNA binding domain. The mouse
     Fkhsf gene spans apprx 14 kb and contains 11 coding exons; the cDNA spans
     a coding region of 1287 bp and encodes a protein of 429 amino acids. The
     human ortholog to mouse Fkhsf cDNA is also provided. Also provided are
     expression vectors suitable for expressing such nucleic acid mols., and
     host cells contg. such expression vectors. Utilizing assays based upon
     the nucleic acid sequences disclosed herein (as well as mutant forms
     thereof), numerous mols. may be identified which modulate the immune
     system.
                                                APPLICATION NO. DATE
                        KIND DATE
     PATENT NO.
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     WO 2000009693 A2 20000224
WO 2000009693 A3 20000615
                               20000224
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FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 21:52:52 ON 31 MAY 2003 292 S TRANSGEN? (L) (SCURFY OR SF OR FKHSF) L1 105 DUP REM L1 (187 DUPLICATES REMOVED) 89 S L2 AND TRANSGENIC L3L443 S L3 AND PY<=1998 43 FOCUS L4 1-L5 L6 3 S L5 AND (SCURFY (L) TRANSGENIC) => d an ti so au ab 16 1-3 1.6 ANSWER 1 OF 3 MEDLINE AN 96152740 MEDLINE Disease in the scurfy (sf) mouse is associated with overexpression of cytokine genes. EUROPEAN JOURNAL OF IMMUNOLOGY, (1996 Jan) 26 (1) 161-5. SO Journal code: 1273201. ISSN: 0014-2980. Kanangat S; Blair P; Reddy R; Deheshia M; Godfrey V; Rouse B T; Wilkinson ΑU The murine X-linked lymphoproliferative disease scurfy is similar to the Wiskott-Aldrich syndrome in humans. Disease in scurfy (sf) mice is mediated by CD4+ T cells. Based on similarities in scurfy mice and transgenic mice that overexpress specific cytokine genes, we evaluated the expression of cytokines in the lesions of sf mice by Northern blotting, quantitative reverse-transcription polymerase chain reaction (RT-PCR) and by hybridization in situ. Overall, the phenotypic characteristics of scurfy disease correlated well with increased interleukin (IL)-4 (lymphadenopathy), IL-6 (B cell proliferation, hypergammaglobulinemia), IL-7 (dermal inflammatory cell infiltration), and high levels of tumor necrosis factor-alpha (wasting). L6 ANSWER 2 OF 3 MEDLINE 95015867 MEDLINE ${\tt CD4+CD8-}\ {\tt T}$ cells are the effector cells in disease pathogenesis in the TIscurfy (sf) mouse. JOURNAL OF IMMUNOLOGY, (1994 Oct 15) 153 (8) 3764-74. Journal code: 2985117R. ISSN: 0022-1767. SO Blair P J; Bultman S J; Haas J C; Rouse B T; Wilkinson J E; Godfrey V L AB Mice hemizygous for the X-linked mutation, scurfy (sf), exhibit a fatal lymphoreticular disease that is mediated by T lymphocytes. To evaluate the respective roles of CD4 or CD8 single positive T cells in scurfy disease, neonates were treated with mAbs directed against the CD4 or CD8 molecules. Whereas mice treated with an anti-CD8 Ab developed lesions and succumbed to disease at the same time (17 days) as their untreated scurfy littermates, mice treated with an anti-CD4 Ab lived up to 11 wk before developing scurfy disease. To insure a more complete elimination of the T cell subsets, the scurfy mutation was bred onto beta 2-microglobulin (beta 2m) -deficient (CD8-less) and CD4-deficient transgenic mouse lines. Whereas there was little moderation of disease in beta 2m-deficient scurfy mice, CD4-deficient scurfy mice had markedly decreased scurfy lesions and a prolonged life span, similar to that of anti-CD4-treated sf/Y mice. Additionally, scurfy disease was transplanted into H-2-compatible nude mice through the adoptive transfer of CD4+CD8- T cells, but not CD4-CD8+ T cells. Flow-cytometric analysis revealed that sf/Y mice have an increased percentage of activated CD4+ T cells in their lymph nodes. In addition, there is an increase in the in vitro production of cytokines in the cultured splenocytes of CD8-less, but not CD4-less, scurfy

mice. These data suggest that CD4+ T cells are critical mediators of

disease in the scurfy mouse.

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